

# AIDS

## MEMORANDUM

Acquired Immune Deficiency Syndrome

National Institute of Allergy and Infectious Diseases

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### GROUND RULES FOR USE OF THE AIDS MEMORANDUM

The AIDS Memorandum serves as a forum for the rapid exchange of new information and ideas among clinicians and scientists involved in AIDS research and management. Material contained in the Memorandum can be of several kinds: positive and/or negative results, clinical and/or experimental findings, preliminary and/or validated data, observations, questions, theories, commentaries, and others. This material is not subjected to peer review. Therefore, users of the Memorandum must agree to treat all material as privileged information and to consider it as tentative and subject to change prior to formal publication in a refereed journal.

Users must agree not to cite material from the Memorandum without first obtaining the consent of the author(s), and, with author permission, to cite information only as a personal communication. Author addresses are provided for this purpose.

Users must agree to contribute data or ideas to the Memorandum at least once a year. On an annual basis, the names of individuals who have not contributed to the Memorandum will be culled from the mailing list, so as to limit circulation of the Memorandum only to individuals actively working in the field.

Finally, users must agree to share material in the Memorandum only with other individuals willing to honor these ground rules.

## AIDS IN EUROPE: EPIDEMIOLOGIC FEATURES

The World Health Organization of Europe (WHO-Europe) and the Danish Cancer Society sponsored a meeting in Aarhus, Denmark, October 19-21, 1983, for European and US AIDS researchers. The meeting was convened in order to summarize the epidemiologic and clinical features of cases of AIDS which have occurred in Europe and to formulate recommendations for public health policies pertinent to AIDS. The meeting was attended by representatives of the national governments and academic institutions from almost every country in Europe. Along with the invitation to attend the meeting, participants had been sent a questionnaire concerning the epidemiology of AIDS. Data from the questionnaires which had been returned were summarized in a manuscript which was distributed, discussed, and amended at the meeting and eventually adopted as the consensus of the participants. Additional data updating case numbers and correcting misunderstandings regarding the diagnosis of AIDS were presented at the meeting.

The total number of cases in Europe which have been diagnosed as AIDS according to the most recent update is 268. An important area of agreement which emerged from the meeting was that the CDC case definition would be used by everyone, at least for the purpose of epidemiologic surveillance. France reported the greatest number of cases (94), followed by the Federal Republic of Germany (42), Belgium (38), the United Kingdom (24), Switzerland (17), Denmark (13), and the Netherlands (12). Eight other countries reported fewer than 10 cases each. Cases of AIDS were reported from all areas of Europe. Two cases were known in Eastern Europe, one

of whom was an African student living there.

As in the United States, AIDS has been diagnosed in Europe with increasing frequency since 1979. According to information contained in the questionnaires, eight cases occurred prior to 1979. (These were reported retrospectively.) During 1982, 67 cases were reported. By the time the conference was held, 104 cases had been reported in 1983.

Of the 200 cases for which detailed information was provided, 74% were individuals of European origin, 21% were individuals of African origin, and 10 were individuals originating from North and Central America (Haiti 8, US 1, and Nicaragua 1). One major difference between the cases evaluated in Europe and those seen in the US was the large number of cases from Africa. To date, 42 African cases have been diagnosed in Belgium, France, Switzerland, and Czechoslovakia. These cases have been in individuals originating mainly from Zaire and other adjacent African countries in the Congo Basin. No African cases have been seen in the United Kingdom, where the large African population originates mostly from West, East, and South African countries. Although the African cases have been diagnosed more frequently in the most recent period, it is unclear from these data whether this represents a referral and recognition bias or a real increase in the occurrence of AIDS in Africa.

Of the cases of AIDS in individuals of European origin, 128/148 (86.4%) could be assigned to a risk group. The distribution of individuals into the various risk groups was similar to the distribution seen in the United States: 80% were homosexual men, 4.8% were hemophiliacs, and 1.4% were heterosexual

drug addicts. In most of the remaining cases, the information provided was inadequate for making a classification.

One hundred eighty-nine of the cases cited in the questionnaires were described by the following clinical diagnoses—opportunistic infections, opportunistic infections and Kaposi's sarcoma, and Kaposi's sarcoma. The distribution of these cases according to the area of origin of the individuals is given in the table.

Diagnosis	All Cases				
	No./Total No. (%)	European	African	Eastern	American
OI only	123/189 (65.1)	86/143	29/36	6/9	2/2
OI and KS	27/189 (14.3)	23/143	2/36	1/9	0/0
KS only	39/189 (20.6)	34/143	3/36	0/9	0/0
Total cases	189	143	36	9	2

Abbreviations: OI, opportunistic infection; KS, Kaposi's sarcoma.

The 34 European cases of Kaposi's sarcoma only were almost exclusively seen in homosexual men.

Further details about the epidemiology, clinical features, and policy recommendations will be published in the *European Journal of Cancer*. The information was collected by WHO and should be considered preliminary until confirmed and published.

Submitted on behalf of the AIDS in Europe—Status Quo 1983 Meeting by R. J. Biggar, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20205.

#### IS AFRICAN KAPOSI'S SARCOMA ENDEMIC AIDS?

It has been assumed that AIDS is a new disease, appearing de novo in the US in 1979. However, there are marked epidemiological similarities between AIDS and the endemic form of Kaposi's sarcoma

(KS) occurring in central Africa. If an infectious agent causing endemic KS in Africa were recently introduced into the US, this could explain how epidemic AIDS emerged in the US.

KS has been a rare tumor in Europe and in the US. In these areas, its prevalence is 0.01-0.06/100,000, and it occurs primarily in older people (Safai B, Good RA: *CA*, 1981, 31:2-12). In a recent update of data regarding the current AIDS epidemic, it was reported that 26% of all US cases have presented with KS alone (*Morb Mort Weekly Rep.*, 1983, 32(35):465-467). This represents well over 500 cases.

In contrast, in central Africa, KS has been a common tumor. KS accounts for 12.8% of all malignant tumors in adults in Zaire, where the highest world wide prevalence of KS is known (Hutt MSR: *Antibiot Chemother.*, 1982, 29:3-8). The epidemiology of KS in Africa, as reviewed by Hutt, showed that this tumor occurred in all the countries bordering Lake Victoria. Within this area, the tumor is most common in males, with a male:female ratio of at least 13:1 in all series. Fifty percent of all cases occur in individuals aged 25-40. There is a small peak for those aged 1-2, and, in this group, the male:female ratio is 1 (Kyalwazi SK: *Antibiot Chemother.*, 1982, 29:59-67). KS is highly area-specific, with marked variations in incidences over short distances; numerous case clusters have been reported. This epidemiology strongly suggests an infectious etiology (Giraldo G, Beth E, Kyalwazi SK: *Antibiot Chemother.*, 1982, 29:12-29). No thorough study of the immunology of African KS has been undertaken. However, it has been observed that immunoglobulin titers were normal while delayed-type hypersensitivity testing was negative in cases of aggres-



sive KS (Master SP, Taylor JF, Kyalwazi, SK, et al: *Br Med J.*, 1970, 1:600-602).

The table lists features of African KS and AIDS KS and demonstrates similarities in the epidemiologies of the two diseases. Although no record was made of opportunistic infections in African KS patients, this population in general has a high incidence of life-threatening infections. A series of post-mortem examinations of Africans dying of KS did demonstrate an unexpectedly high incidence of infection as a cause of death, including pulmonary infection and dysentery (Templeton A: *Cancer*, 1972, 30:854-867).

COMPARISONS OF AFRICAN KS AND AIDS

Feature	African KS	AIDS
Sex ratio (M:F)	13:1	14:1
Age	Small peak 2-3 yr; increase after 20 yr; median 25-40 yr	Small peak 1-2 yr; increase after 20 yr; median 30-39 yr
Geographical distribution	Equatorial Africa; highly area-specific	USA, Europe; highly area-specific
Social distribution	All tribal groups; upper/lower classes	All ethnic groups; all classes
Infectivity	Clustering	Clustering; sexually transmitted; blood borne
Associated infections	CMV; KSV; EBV; KHV; Eh	CMV; KSV; EBV; KHV; Eh; syphilis
Opportunistic infections	Not recorded; ? Mixed	50% PCP; 25% Other
Humoral immunity	Normal	? Normal
Cellular immunity	DTM absent	DTM absent; lymphopenia; T helper deficit

Abbreviations: CMV, cytomegalovirus; KSV, herpes simplex virus; EBV, Epstein-Barr virus; KHV, hepatitis B virus; Eh, *Entamoeba histolytica*; PCP, *Pneumocystis carinii* pneumonia; DTM, delayed type hypersensitivity.

If African KS is an infectious disease, what accounts for the high male:female ratio in the adult cases? Such a pattern can be seen in infectious diseases where males and females have dif-

ferential occupational exposures, as is the case for cutaneous Leishmaniasis in Mexico. However, Hutt was unable to demonstrate such a difference in the life styles between the sexes in Uganda.

How prevalent homosexuality is in central Africa is unknown. However, this area has the highest incidence of polygamy in the world, and delayed marriage for males is common (Dr. P. Spencer, personal communication). Because a large number of post-adolescent males are denied access to young females, homosexual contact is thought to occur before later heterosexual marriage. If African KS is caused by a sexually transmitted factor, then homosexuality in the young adult group could explain the pattern of the tumor in this population. The smaller number of childhood cases could be explained by vertical transmission.

A putative agent causing KS in Africa could have been introduced into a susceptible population in the US, possibly carried by homosexual visitors to East Africa. The recent reports of AIDS in Zaire and of 59 cases of AIDS in Europe whose only risk factor was exposure to central Africa strengthen the links between AIDS and African KS. If AIDS is an epidemic form of endemic KS, then closer examination of the disease in Africa will answer many questions on the course and cause of this mysterious disease.

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#### THE INCIDENCE OF KAPOSI'S SARCOMA IN THE US AND PUERTO RICO, 1973-1981

The epidemiology of Kaposi's sarcoma (KS) has attracted considerable interest

because of the many cases associated with AIDS. The AIDS outbreak, which includes both opportunistic infections and KS, was first recognized in 1981, although, in retrospect, cases began to appear somewhat earlier. While several high-risk groups have been identified, most of the AIDS cases have occurred among young homosexual men.

Using data from the Surveillance Epidemiology End Results (SEER) program of the National Cancer Institute, we examined the incidence of KS in the US and Puerto Rico. The incidence of KS in 1973-79 was found to be higher than is usually cited for the pre-epidemic KS incidence rate: 0.29 male and 0.07 female cases per 100,000 per year. Collectively, the nine SEER registries in the US showed only a slight increase in the incidence of KS between 1973-79 and 1980-81. However, the SEER registry covering San Francisco, where a large number of AIDS cases have occurred, showed a marked increase in KS in 1981.

The incidence rates of KS in the SEER registry of Puerto Rico were generally higher than those in the US registries, despite data which suggested that KS may be underreported. The demographic characteristics of KS in Puerto Rico suggested the classical rather than the AIDS-related form of KS. Puerto Rico and perhaps other Caribbean islands may be endemic areas of KS.

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#### FACTOR VIII, KAPOSI'S SARCOMA AND AIDS

Our autopsy observations on 26 victims of AIDS indicate that, in virtu-

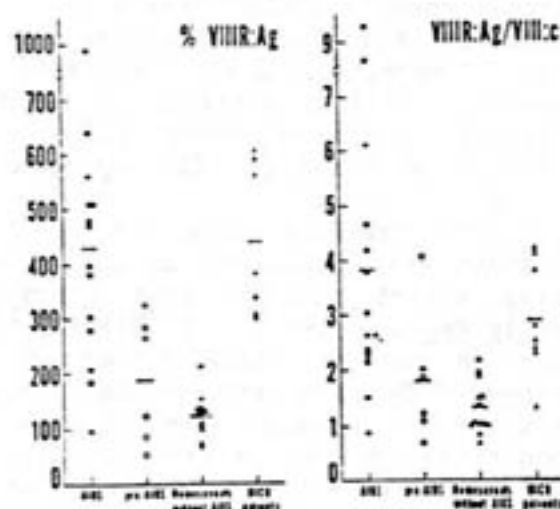
ally every case, generalized (lymphadenopathic) Kaposi's sarcoma (KS), a tumor thought to be of endothelial origin, is present (data to be published). We have also observed KS lesions in biopsy specimens of lymph nodes in a high proportion of AIDS patients. Since coagulation factor VIII has been shown to be associated with the neoplastic cells of KS (Nadji M, Morales AR, Ziegler-Weissman J, et al: Arch Pathol Lab Med., 1981, 105:274-275), we hypothesize that factor VIII may be elevated in the peripheral blood of AIDS patients.

The molecular complex of factor VIII consists of at least two subunits, the von Willebrand-related antigen (VIII:Ag) which is produced chiefly by endothelial cells and a procoagulant (VIII:c) which is synthesized by the liver. If the common denominator of AIDS is KS and if KS cells contribute to an elevation of factor VIII in the blood, we would further speculate that levels of VIII:Ag in the blood of AIDS patients would rise disproportionately compared to levels of VIII:c. Accordingly, we have measured levels of these factor VIII subunits in blood of AIDS patients and controls.

Thirty-three patients were studied. Fourteen were diagnosed as having AIDS using strict CDC criteria (Morb Mort Weekly Rep., 1982, 31(37):507-514). Thirteen patients were homosexual men without AIDS (some of whom had generalized lymphadenopathy). Six patients were homosexual men with a pre-AIDS syndrome defined by having at least four of the following symptoms or characteristics: fever of unknown origin, weight loss and/or diarrhea, lymphadenopathy, skin test anergy, lymphopenia (less than 1,500 lymphocytes per cubic mm), oral thrush, greater than 1,000 different sexual partners, multiple infections,

inverted T-helper to T-suppressor lymphocyte ratio. In addition, assays were performed on the blood of seven patients who were hospitalized in our medical intensive care unit (MICU) for serious acute illnesses unrelated to AIDS. This group provided data, previously unavailable, on the ratio of VIIIIR:Ag to VIII:c in acute disease (factor VIII is an acute phase reactant).

Measurements of levels of peripheral blood factor VIII:c and VIIIIR:Ag were made using standard methods (Miale JB: in Mosby CV (Ed): Laboratory Medicine Hematology, 6th ed, St. Louis, 1982, 929-932). Data are presented in the figure in two ways. The concentration of VIIIIR:Ag is expressed as % of normal expected values (normal values are in the range of 50-150%). The ratio of VIIIIR:Ag/VIII:c is given directly (with ratios for normals approximately = 1).



There were marked elevations in both the % VIIIIR:Ag and the VIIIIR:Ag/VIII:c ratios in patients with AIDS, although, for both parameters, the ranges of values were large. There were more modest

elevations in the % values and ratios obtained for pre-AIDS subjects. Homosexuals without AIDS had % values and ratios within normal limits. The % values and ratios also were elevated in the acutely ill patient subset. The differences in the values and ratios for AIDS patients and MICU patients were not significant and do not support a conclusion that the rises measured can be related directly to KS. In order to further assess the value of these assays for determining the presence and/or ubiquity of KS in AIDS, we are currently studying serially the blood of various patient groups, including persons with KS but without opportunistic infections.

Note added in proof: The pre-AIDS patient with the highest ratio shown in the figure (= 4) has recently developed overt AIDS. Another patient who had originally been in the pre-AIDS group developed AIDS during the study and was transferred to the AIDS category at that time. Because these two patients had the two highest values in their original subset, high ratio values may prove to be predictive of AIDS development.

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#### CYCLOSPORINE-LIKE SUBSTANCES NOT DETECTED IN AIDS PATIENTS

It has been suggested recently that AIDS may be caused by the "systemic release of a potent cyclosporin-like immunosuppressive molecule from a chronic fungal infection in AIDS patients" (Sell KW, Folks F, Kwon-Chung KJ, et al: N Engl J Med., 1983, 309:1065). This suggestion was based on analogies between



immunosuppressive effects produced by cyclosporine and changes in immune status which are characteristic of AIDS and by high-performance liquid chromatography (HPLC) analyses of AIDS plasma.

Cyclosporine has a unique cyclic undecapeptide structure (Ruegger A, Kuhn M, Lichti H, et al: Helv Chim Acta, 1976, 59:1075-1092). Analytical techniques for detecting cyclosporine include radioimmunoassay (RIA) (Donatsch P, Abisch E, Homburger M, et al: J Immunoassay, 1981, 2:19-32) and several HPLC methods (Neiderberger W, Schaub P, Beveridge T: J Chromatogr., 1980, 182:454-458; Carruthers SG, Freman DJ, Koegler JC, et al: Clin Chem., 1983, 29:180-183; Yee GC, Gmur TJ, Kennedy MS: Clin Chem., 1982, 28:2269-2271; Sawchuk RJ, Cartier LL: Clin Chem., 1981, 27:1368-1371). The RIA is sensitive to the cyclic undecapeptide structure only. However, there is a sufficiently broad spectrum of cross-reactivity in this assay that cyclosporine-like compounds possessing an intact cyclic structure but having different substituents on the ring are measured together with cyclosporine. The HPLC techniques are specific for cyclosporine, but are plagued by the presence of co-eluting peaks due to endogenous plasma components. Even column switching techniques do not completely eliminate this problem (Smith HT, Robinson WT: J Chromatogr., 1984, 305:in press).

We have analyzed samples of blood, plasma, and serum for cyclosporine using RIA and HPLC techniques. Samples were tested from six patients who fulfilled the Centers for Disease Control criteria for diagnosis of AIDS, two patients who were classified as having the AIDS prodrome and, for control purposes, 15 AIDS-free patients, 10 of whom belonged to several AIDS "risk groups."

The sensitivities of the analytical

methods were verified by analyses of cyclosporine-positive blood specimens from a normal, healthy volunteer who had been entered into a study assessing the dose-proportionality of cyclosporine (Abolin CR, et al: Study No. 40, Volumes 3.80-3.84, Section 12(h) of Cyclosporine (Sandimmune™) New Drug Application). His blood samples had been stored for 1 year at -20°C.

All samples were analyzed blind. Sample aliquots for RIA were fortified with normal human blood to eliminate matrix differences between the blood, plasma, and serum specimens; all samples were then diluted and analyzed according to instructions provided with the cyclosporine RIA kit (Cyclosporin RIA-Kit Instructions, 1st ed, 14 Feb 1983, Sandoz Ltd., Switzerland). For the HPLC analyses, aliquots of blood or plasma samples were extracted with diethyl ether, and the extracts were chromatographed according to the conditions of Carruthers et al. (ref. above). Their method was chosen as the one most likely to coextract and chromatograph "cyclosporine-like" materials. The HPLC eluate was collected starting at several minutes before the retention time for dihydrocyclosporine C and ending with the retention time for cyclosporine D. Both compounds are used as internal HPLC standards, and their retention times bracket those of cyclosporine A. Therefore, any cyclosporine-like compounds in the samples should be eluted in this window. The HPLC eluates were evaporated, the residues reconstituted with small volumes of RIA buffer containing surfactants to enhance redissolution, and the concentrates analyzed by RIA.

All samples from the positive control volunteer showed a positive RIA response. The concentration data obtained in this analysis showed less than 10%

difference from data obtained 1 year ago, validating the RIA and also demonstrating the stability of cyclosporine in frozen blood. In contrast, we detected no cyclosporine or cyclosporine-like substances in either patient or control samples above the limit of quantitation of the RIA (conservatively set at 30 ng/ml). Analysis of variance of RIA responses between AIDS and control samples showed that there were no statistically significant differences. These analyses suggest that cyclosporine or cyclosporine-like substances are absent at concentrations less than 30 ng/ml as well.

In the UV tracings of the HPLC analyses for both control and AIDS samples, we noticed various and variable peaks that are known to arise from endogenous extractable materials. We did not find any peaks in the AIDS samples that were unique to and limited to this subgroup. All samples known to contain cyclosporine showed cyclosporine peaks in the chromatograms consistent with the expected concentration of cyclosporine (corrected for extraction and recovery methods). RIA analyses of all HPLC fraction concentrates were negative for the control and AIDS samples but positive for the samples known to contain cyclosporine.

We take no issue with the hypothesis that systemic release of an immunosuppressive agent by an invading fungus may be a possible cause of AIDS. Our data indicate, however, that the putative immunosuppressive agent in the blood of AIDS patients is neither cyclosporine nor cyclosporine-like.

This note includes information contained also in a letter which has been accepted for publication in The New England Journal of Medicine.

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ter, W. A. Krivoy, J. Raskova, and K. Raska, Jr. Pharmaceutical Research and Development, Sandoz, Inc., East Hanover, New Jersey 07936 and Department of Pathology, University of Medicine and Dentistry of New Jersey-Rutgers Medical School, Piscataway, New Jersey 08854.

#### NON-TRANSMISSION OF AIDS BETWEEN SEXUAL PARTNERS

This study describes clinical and laboratory analyses of a bisexual man with AIDS and of his wife. Despite continued sexual activity, the transmission of AIDS or of any measurable immunodeficiency has not occurred to date between these two sexual partners.

A 42-year-old man presented with Pneumocystis carinii pneumonia after a 2 month prodrome of malaise, fever, anorexia, and a 10 lb weight loss. The patient's lymphocyte count was 850 per mm<sup>3</sup>, of which 585 (69%) were T cells. There were 99 OKT4+ cells and 474 OKT8+ cells per mm<sup>3</sup> (OKT4:OKT8 = 0.21). He was anergic to four cutaneous recall antigens (candida, trichophyton, mumps, and diphtheria-tetanus toxoid). He was seropositive for cytomegalovirus (CMV) antibody by ELISA analysis, and CMV was isolated from his urine. However, there was no blastogenic response to CMV. Blastogenesis to phytohemagglutinin (PHA) was normal. The patient received sulfamethoxazole-trimethoprim therapy and transient respirator support. Eight weeks later, his immunologic status was unchanged, but he appeared outwardly well.

The patient had been married for 18 years. Sexual activity with his wife was limited to kissing, manual genital contact, and penile-vaginal intercourse. Intercourse occurred once or twice a



week in the 5 years preceding the patient's illness. The wife corroborated this history.

The patient had had several experimental homosexual encounters from the time he was 14 until he was 18 years old. He resumed homosexual activity at age 32, usually meeting anonymous partners in parks or public rest rooms. He had a total of about 50 such contacts, averaging 3-5 per year in the 3 years preceding his illness. Most of these involved mutual orogenital contact, although active or receptive anal intercourse occasionally occurred. Several of the homosexual encounters had occurred in or near San Francisco. The patient had had hepatitis B 10 years before the onset of his current illness, and an assay for anti-HBs antibody was positive. The fluorescent treponemal antibody absorption test was also positive; the VDRL was nonreactive. The patient denied having had other sexually transmitted diseases (STD) and had never received a transfusion or blood products.

The wife, age 40, gave a history of lifelong monogamy and had no history of STD or transfusion. She was examined 8 weeks after her husband's illness (4 months after the onset of his prodromal symptoms). She was asymptomatic and had a normal physical examination. She was seropositive for anti-CMV antibody, but cultures of her urine, cervix, rectum, and pharynx were negative for CMV. The lymphocyte count was 1,598 per  $\text{mm}^3$ , of which 1,374 (86%) were T cells. There were 605 OKT4+ lymphocytes and 179 OKT8+ lymphocytes per  $\text{mm}^3$  (OKT4:OKT8 = 3.38). Her lymphocytes showed normal blastogenic responses to CMV and PHA. Positive skin reactions were measured to the mumps recall antigen (54 mm induration) and to candida (4 mm). There was no response to trichophyton or diphtheria-

tetanus toxoid. The wife remains well 8 months later but has declined to undergo further immunologic and virologic testing.

Sexual transmission of AIDS is suspected on several epidemiologic grounds, including observations that the sexual partners of AIDS patients commonly have subclinical cellular immunodeficiencies or, occasionally, overt AIDS. These observations have been made primarily in homosexual men. However, many homosexual men without AIDS have subclinical immunologic abnormalities. Therefore, the relationship of immunodeficiency to specific sexual contacts or activities is not yet clear.

In this study, AIDS and immunodeficiency were not transmitted from a bisexual man to his wife. There are several possible explanations for the normal clinical and immunologic status of the wife; they are not mutually exclusive. AIDS may not be caused by a specific transmissible agent, the putative etiologic agent of AIDS may not yet have been transmitted from the patient to his wife, the evaluation of the wife may have been carried out during an incubation period, or the wife may have had a subclinical infection with the putative AIDS agent, perhaps with the development of a protective immune response. Further attempts to reexamine the wife are underway.

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# T-LYMPHOCYTE SUBSET ABNORMALITIES IN HEMODIALYZED ADULTS WHO HAVE RECEIVED BLOOD TRANSFUSIONS

Adults on chronic maintenance hemodialysis who have received blood transfusions show prolonged renal allograft survival which appears to be correlated with defective cell-mediated immunity (Watson MA, Briggs JD, Diamandopoulos AA, et al: Lancet, 1979, 2:1323-1326). To study this phenomenon, we examined the peripheral blood lymphocytes (PBL) of 29 hemodialyzed adults, 19 of whom had received blood transfusions (BT) and 10 of whom had not (NT). Data were also obtained on more than 40 age-matched normal volunteers.

		Controls	BT	NT
PBL	$\text{L/mm}^3$	29.7 $\pm$ 1.6 1989 $\pm$ 104	28.9 $\pm$ 3.3 1441 $\pm$ 172	33.5 $\pm$ 1.8 2331 $\pm$ 401
OKT3+	$\text{L/mm}^3$	69.1 $\pm$ 1.6 1323 $\pm$ 86	64.2 $\pm$ 3.6 918 $\pm$ 118	60.5 $\pm$ 3.7 <sup>a</sup> 1433 $\pm$ 255
OKT4+	$\text{L/mm}^3$	48.1 $\pm$ 1.1 924 $\pm$ 64	35.5 $\pm$ 3.1 <sup>b</sup> 486 $\pm$ 60	44.7 $\pm$ 3.3 1062 $\pm$ 225
OKT8+	$\text{L/mm}^3$	26.4 $\pm$ 1.0 504 $\pm$ 36	30.9 $\pm$ 2.7 483 $\pm$ 96	27.5 $\pm$ 3.1 619 $\pm$ 88
OKT4+/OKT8+		1.98 $\pm$ 0.10	1.35 $\pm$ 0.20 <sup>a</sup>	1.87 $\pm$ 0.27

<sup>a</sup>  $p < 0.05$ , <sup>b</sup>  $p < 0.01$ , <sup>c</sup>  $p < 0.001$ , <sup>d</sup>  $p < 0.0001$  as compared to control subjects.

When compared with controls, recipients of BT showed statistically significant decreases in the absolute numbers of OKT3+ cells, the percent representation and absolute numbers of OKT4+ cells, and the OKT4+/OKT8+ ratio. These findings are similar to those seen in other individuals who have received BT (Kessler CM, Schulof RS, Goldstein AL, et al: Lancet, 1983, 1:991-992). The NT subjects showed decreases only in the percent representations of OKT3+ cells.

We wish to emphasize that none of the subjects of this study, including those

with depressed numbers of OKT4+ cells, have signs or symptoms associated with AIDS, such as unexplained fevers, weight loss, or lymphadenopathy. These data, however, may explain both the decrease in cell-mediated immunity in transfused hemodialyzed subjects and their decreased renal allograft resistance. These changes may also have relevance to cases of AIDS developing in those individuals who have been exposed to blood or blood products.

Whether these changes were induced by the transfusions or are present as a result of the generalized hypofunction of the bone marrow is not known. A prospective study is currently underway to help determine the pathogenic effects of BT and will be reported in a future issue of the Memorandum.

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## AIDS AND FLOW CYTOMETRY: CALL FOR PAPERS

A workshop on AIDS and Flow Cytometry, sponsored by the National Institute of Allergy and Infectious Diseases (NIAID), will be held April 3, 1984, at the Bethesda Marriott Hotel. This meeting will precede a meeting on Flow Cytometry which is being held by the Becton Dickinson Company on April 4-5 at the same place. Anyone with data to present at a session on AIDS and FACS should contact Dr. Thomas Folks, NIAID, Building 10, Room 11C216, Bethesda, Maryland 20205, (301) 496-4553 or Dr. Thomas Chused, NIAID, Building 5, Room 228, Bethesda, Maryland 20205, (301) 496-2789.

# SPECIFICITY OF LYMPHOCYTOTOXIC ANTIBODIES IN AIDS AND PRE-AIDS PATIENTS

Antilymphocyte antibodies have been detected in AIDS patients, but, to our knowledge, no reports have been published on the specificities of such antibodies for subpopulations of T lymphocytes. This report describes the reactivity of lymphocytotoxic antibodies (LCA) with T helper, T suppressor, and non-T mononuclear cells in patients with AIDS and patients with pre-AIDS symptoms.

Thirteen patients (3 with AIDS, 10 with pre-AIDS symptoms), 6 healthy homosexual controls, and 17 healthy heterosexual controls were the subjects of this study. Of the 13 patients, five were drug addicts (3 males, 2 females) and 8 were male homosexuals. Blood was collected from all individuals. One portion was heparinized for cellular studies, and another portion was allowed to coagulate for studies of sera. Mononuclear cells from patients and controls, fractionated using Ficoll-Hypaque, were typed by an indirect immunofluorescence technique using various monoclonal antibodies: OKT3 (a pan T cell marker), OKT4 (a T helper/inducer cell marker), and OKT8 (a T suppressor/cytotoxic cell marker). Sera from patients and controls were examined for LCA using a microcytotoxic test which was a modification of the Terasaki technique (Mottironi VZ, Terasaki PI: in Terasaki, PI (Ed): Histocompatibility Testing, Munksgaard, Copenhagen, 1970, 301-308). Target cells for these studies were preparations of either purified T cells, T helper cells, T suppressor cells, or a mixture of B cells plus macrophages from healthy donors. The results of cytotoxic assays were expressed as the cytotoxic index

(CI) ( $100 \times \% \text{ dead cells in test sample} / \% \text{ dead cells in control}$ ). Values for control, positive samples were usually in the range of 90-95% dead cells. A CI  $\geq 20\%$  was considered positive for LCA, while a CI  $\leq 20\%$  was considered negative.

Lymphocytotoxic antibodies were detected in all of the symptomatic individuals (AIDS and pre-AIDS groups) but in only one (6%) of the healthy heterosexual controls and in none of the healthy homosexual controls. Titers of lymphocytotoxic antibodies in the patients ranged from 125-625. The antibodies were detected at 15°, 20°, and 37°C, but the reactivity at 37°C was 20-40% lower than at 15°C. Antibodies from all of the patients reacted with both T helper and T suppressor cells, but in nine of the 13 serum samples the reaction was higher with the T helper cells ( $p < 0.05$ ). No correlation could be found between the levels of T helper lymphocytes or the T helper/T suppressor cell ratio and the levels of lymphocytotoxic antibodies in patients ( $p > 0.1$ ). Sera of seven patients and three of nine healthy heterosexual controls tested reacted with non-T mononuclear cells (B cells plus monocytes). The degree of cytotoxicity with these cells did not correlate with the levels of lymphocytotoxic antibodies to T cells.

Two new findings have emerged from these studies: LCA react with both purified T helper and T suppressor cell preparations and both homosexual men with AIDS and drug addicts with AIDS have LCA which demonstrate these specificities.

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AIDS CASES REPORTED TO THE CENTERS FOR DISEASE CONTROL AS OF JANUARY 23, 1984

UNITED STATES CASES

DISEASE	CASES	PERCENT OF TOTAL	DEATHS	PERCENT DEAD
KS without PCP	858	26.0	198	23.1
PCP without KS	1695	51.2	809	47.7
Both KS and PCP	225	6.8	145	64.4
OI without KS or PCP	530	16.0	280	52.8
TOTAL	3308	100.0	1432	43.3

KS = Kaposi's sarcoma      PCP = Pneumocystis carinii pneumonia  
OI = Opportunistic infections

RISK GROUPS*	MALES		FEMALES		TOTAL	
	CASES	% OF TOTAL	CASES	% OF TOTAL	CASES	%
Homosexual or bisexual	2355	76.3	0	0.0	2355	71.2
IV drug user	462	14.9	120	54.3	582	17.6
Haitian	126	4.1	21	9.5	147	4.5
Hemophiliac	21	0.7	0	0.0	21	0.6
No apparent risk group or unknown	123	4.0	80	36.2	203	6.1
TOTAL	3087	100.0	221	100.0	3308	100.0

\* The risk groups listed are hierarchically ordered; cases with multiple risk factors are tabulated only in the risk group listed first.

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**References:** References should be integrated into the text in parentheses. Each citation should include journal title, year of publication, volume and issue numbers and inclusive page numbers. Citations from books should include book title, editor(s), publisher, year of publication and relevant page numbers.

**Tables:** Whenever possible, data should be organized into tables rather than figures.

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